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STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.
1100 NEW YORK AVE., N.W.
WASHINGTON, DC 20005

EXAMINER

SLOBODYANSKY, ELIZABETH

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 11/25/2003

29

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/974,973

Applicant(s)

HANKE, PAUL D.

Examiner

Elizabeth Slobodyansky

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 August 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3 and 5-23 is/are pending in the application.
- 4a) Of the above claim(s) 9-11 and 14-18 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,5-8,12,13 and 19-23 is/are rejected.
- 7) ☒ Claim(s) 3 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 22 August 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
- a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

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DETAILED ACTION

The amendment filed August 22, 2003 amending the specification to delete references to the duplicate sequences, amending claims 1, 2, 19, canceling claim 4 and adding claims 21-23 has been entered.

The statement regarding the biological Deposit Number NRRL B-30293 is given in the paragraph bridging pages 28-29 of Remarks.

Claims 1-3 and 5-23 are pending. Claims 9-11 and 14-18 are withdrawn.

Drawings

The substitute drawings filed on August 22, 2003 have been approved by Draftsman and examiner.

Specification

The instant disclosure contains sequence disclosure that is encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825. 37 CFR 1.821(c) requires that "The sequence identifiers must begin with 1 and increase sequentially by integers" (MPEP 2422.03).

The substitute Sequence Listing filed August 22, 2003 indicates total of 19 sequences while it contains only 17. It does not contain SEQ ID NOs: 3 and 4.

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Applicants are required to submit a substitute corrected Sequence Listing and a computer readable form thereof accompanied by the amendment to the specification.

The description of figures on page 4 is objected because of the following:

in the description of Figure 2, there is no sequence identifier of the wild-type pyruvate carboxylase. Amending the description to refer to "the amino acid sequence of the wild-type pyruvate carboxylase (SEQ ID NO:19). The specific changes corresponding to the amino acid sequence of the feedback-resistant pyruvate carboxylase (SEQ ID NO:2) are indicated", for example, is suggested.

The description of Figures 3-5 refer to "*C. glutamicum* NRRL B-11474" while the figures show "BF100".

The specification is objected to because it states "a nucleotide sequence which encodes the amino acid sequence of SEQ ID NO:2, or the amino acid sequence encoded by the DNA contained in Deposit Number NRRL B-11474" (page 3) and "The nucleic acid sequence shown in Figure 1 (SEQ ID NO: 1), or to the nucleic acid sequence of the deposited DNA (NRRL B-30293, deposited May 30, 2003)" (page 6). Since SEQ ID NO:1 encodes SEQ ID NO:2, referring to two different deposit numbers is confusing. Furthermore, Deposit Number NRRL B-11474 is *Corynebacterium glutamicum* (page 18), whereas Deposit Number NRRL B-20293 is *E. coli* (Viability

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statement provided by Applicants on August 22, 2003). Nowhere the specification discloses the relationship between deposits "*C. glutamicum* NRRL B-11474" and "*E. coli* NRRL B-30293". Furthermore, the experimental data presented in Tables and Figures refer to *C. glutamicum* NRRL B-11474 and not to *E. coli* NRRL B-20293.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 5-8, 12, 13, 19, 20 and 21-23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1, with dependent claims 5-8, 12 and 13, is directed to a nucleic acid encoding a mutant pyruvate carboxylase that is desensitized to feedback inhibition by aspartic acid, said mutant pyruvate carboxylase having an amino acid sequence containing at least one mutation selected from the group consisting of seven specific mutations in SEQ ID NO:19.

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Claim 21 is drawn to a nucleic acid encoding a pyruvate carboxylase containing at least one mutation which desensitizes said pyruvate carboxylase to feedback inhibition by aspartic acid, said nucleic acid hybridizes under stringent conditions to a second nucleic acid comprising at least one mutation in SEQ ID NO:19, selected from the group consisting of seven specific mutations.

Because “containing” and “comprising” is open language, the number of allowed mutations is not limited in terms of the mutant’s sequence homology to SEQ ID NO:19. Therefore, the nucleic acid claimed in both claim 1 and claim 21 is not limited to the structure homologous to SEQ ID NO:1 and amounts to any structure.

The specific recited mutations constitute less than 1% of the entire SEQ ID NO:19 that is 1140 amino acid long.

The specification does not contain any disclosure of the structures of all mutant pyruvate carboxylases containing the specific mutations that are desensitized to feed back inhibition by aspartic acid. The genus of proteins that comprise these molecules is a large variable genus comprising many structurally diverse proteins. The specification discloses only a single species of the claimed genus, a mutant pyruvate carboxylase comprising all seven specific mutations and having the amino acid sequence of SEQ ID NO:2. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the “functionality” of being “desensitized to feed back inhibition by aspartic acid” and fails to provide any structure:

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function correlation present in all members of the claimed genus. Therefore, the specification is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claims 19 and 20 are directed to nucleic acid molecules encoding a genus of polypeptides of any structure and function comprising SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16 or SEQ ID NO:18. Said sequences are 13-18 amino acids in length. The specification does not contain any disclosure of the function of all DNA sequences encoding polypeptides that comprise SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16 or SEQ ID NO:18. The genus of DNAs that comprise these above DNA molecules is a large variable genus with the potentiality of encoding many different proteins. The genus of claimed DNAs encodes polypeptides retaining the requisite pyruvate carboxylase activity and polypeptides of unknown function. Therefore, many functionally unrelated DNAs are encompassed within the scope of these claims, including partial DNA sequences. The specification discloses only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. One skilled in the art

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cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claim 22, with dependent claim 23, is drawn to a nucleic acid that hybridizes under stringent conditions to SEQ ID NO:2. There is no limitation on the function of an encoded polypeptide.

The specification does not contain any disclosure of the function of all DNA sequences that hybridize under stringent conditions to SEQ ID NO:2. The genus of said nucleic acid molecules is a large variable genus with the potentiality of encoding many different proteins. Therefore, many functionally unrelated DNAs are encompassed within the scope of these claims, including partial DNA sequences. The specification discloses only two species of the claimed genus encoding pyruvate carboxylases of SEQ ID NO:2 and SEQ ID NO:19 having different properties which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. One skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claim 2 is drawn to a nucleic acid molecule comprising a nucleotide sequence encoding the amino acid sequence encoded by the DNA contained in Deposit Number NRRL B-20293. The specification as originally filed referred interchangeably to Deposit numbers NRRL B-20293 and NRRL B-11474 as encoding the same sequences, *supra*. With the amendment of August 22, 2003 Applicants provided Viability statement

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disclosing Deposit Number NRRL B-20293 as *E. coli*. While the enablement requirement is satisfied by the Deposit and Applicants' statement, the specification still must contain the description of what the deposit contains.

Claims 1, 5-8, 12, 13, 19, 20 and 21-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a DNA encoding SEQ ID NO:2, including SEQ ID NO:1, and a DNA that hybridizes under stringent conditions to SEQ ID NO:1 and encodes a pyruvate carboxylase containing at least one mutation corresponding to at least one of seven specific mutations in SEQ ID NO:19 which desensitizes said pyruvate carboxylase to feedback inhibition by aspartic acid, does not reasonably provide enablement for a DNA encoding a mutant pyruvate carboxylase that is desensitized to feedback inhibition by aspartic acid, said mutant pyruvate carboxylase having an amino acid sequence of unknown homology to SEQ ID NO:19 containing at least one (or seven) specific mutations and for a DNA that hybridizes thereto under stringent conditions. It does not reasonably provide enablement for a nucleic acid that hybridizes under stringent conditions to a nucleic acid encoding SEQ ID NO:2 and encodes a polypeptide of an unknown function and for a nucleic acid having an unknown homology to SEQ ID NO:1 and encoding pyruvate carboxylase or a polypeptide of an unknown function comprising a fragment of SEQ ID NOs: 6, 8, 10, 12, 14, 16 or 18. The specification does not enable any person skilled in the art to which it

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pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The stringent hybridization conditions are defined in the specification as comprising the wash step in 0.1xSSC at 65° C (page 8, paragraph 26).

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) considered in determining whether undue experimentation is required, are summarized the predictability or unpredictability of the art, and (8) the breadth of the claims.

Factors pertinent to this discussion include predictability of the art, guidance in the specification, breadth of claims, and the amount of experimentation that would be necessary to use the invention.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of mutants broadly encompassed by the claims, *supra*. The claims encompass nucleic acids encoding pyruvate carboxylase with the requisite property having an unknown homology to SEQ ID NO:1.

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The specification teaches a DNA of SEQ ID NO:1 that encodes a mutant pyruvate carboxylase with seven specific mutations relative to the wild-type sequence of SEQ ID NO:19. The specification does not teach any pyruvate carboxylase mutants that comprise in addition to the requisite mutations other mutations and exhibit the requisite property. Further, it fails to provide information regarding other combinations of substitute amino acids that would result in a mutant with the requisite characteristics. While there is a great number of possible mutants, it is *a priori* unpredictable as to which mutant will exhibit the claimed property. Therefore, the breadth of these claims is much larger than the scope enabled by the specification.

The amino acid sequence of a protein determines its structural and functional properties, and predictability of what changes in the amino acid sequence can be tolerated and result in similar activity is extremely complex, and well outside the realm of routine experimentation, because accurate predictions of a protein's structure from mere sequence data are limited. Furthermore, while recombinant techniques are available, it is not routine in the art to screen large numbers of peptide mutants where the expectation of obtaining similar activity is unpredictable based on the instant disclosure.

The specification does not support the broad scope of the claims which encompass polynucleotides with unknown homology to SEQ ID NO:1 encoding a pyruvate carboxylase with the requisite property because the specification does not

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establish: (A) regions of the protein structure which may be modified without effecting the requisite pyruvate carboxylase activity; (B) the general tolerance of said pyruvate carboxylase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any pyruvate carboxylase residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Therefore, one of ordinary skill would require guidance, such as information regarding the specific amino acid changes that would render a pyruvate carboxylase desensitized to feedback inhibition by aspartic acid, in order to make a mutant pyruvate carboxylase with the requisite property other than a mutant pyruvate carboxylase of SEQ ID NO:2 in a manner reasonably correlated with the scope of the claims. Without such guidance, the experimentation left to those skilled in the art is undue.

Furthermore, claims 19, 20, 22 and 23 encompass DNAs encoding polypeptides of unknown function in addition to polypeptides with the requisite pyruvate carboxylase activity. It would require undue experimentation to establish the function of all polypeptides comprising the recited fragments. Without knowing the function of a polypeptide, it is impossible to know how to use it and a DNA encoding thereof.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 21, with dependent claim 23, is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 21 recites "at least one mutation which desensitizes said pyruvate carboxylase". It is unclear whether a mutation other than a mutation corresponding to one of the seven specific mutations in SEQ ID NO:19 is encompassed by the claim.

Furthermore, claim 21 is confusing as containing clauses numbered not from a) but from h).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in-

(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or

(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

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Claims 22 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Koffas et al.

Koffas et al. (GenBank accession AF038548, December 24, 1997) discloses a 3637 bp DNA encoding a pyruvate carboxylase from *C. glutamicum* having the amino acid sequence that is 100% identical to SEQ ID NO:19 of the instant invention. As such it will hybridize to a nucleic acid encoding SEQ ID NO:2 under the stringent conditions comprising the wash step at 65° C.

Claims 22 and 23 are rejected under 35 U.S.C. 102(e) as being anticipated by Sinskey et al.

Sinskey et al. (US Patent 6,171,833) discloses SEQ ID NO:1 encoding a pyruvate carboxylase from *C. glutamicum* having the amino acid sequence of SEQ ID NO:2, said amino acid sequence 100% identical to SEQ ID NO:19 of the instant invention. As such it will hybridize to a nucleic acid encoding SEQ ID NO:2 under the stringent conditions comprising the wash step at 65° C.

Allowable Subject Matter

Claim 3 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

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Response to Arguments

Applicant's arguments filed August 22, 2003 have been fully considered but they are not persuasive.

The examiner clarifies that no rejection under 35 USC 101 was made in the previous Office action. Only the heading was used. The warning was made that "should claim 3 be found allowable, claim 4 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof". Nowhere the Office action stated that claim 3 is rejected. (Office action mailed April 22, 2003, page 6).

With regard to the 112, 1st paragraph, rejections, Applicants refer to the review by Modak et al. and the paper by Attwood (both cited on form PTO-1449 filed August 19, 2002) to state that "there is a great deal of conservation among different enzymes of this class from different species" (Remarks, page 23). Applicants also state that 'the specification and claim should specify a limit on the number of amino acid substitutions, deletions, insertions and/or additions that may be made to a sequence, in the present case, SEQ ID NO:2 and or to the non-mutated SEQ ID NO:19. The specification and claim indicates what distinguishing attributes shared by the members of the genus. The reference by Attwood, incorporated by reference into the specification specifies a limit on amino acid substitutions, deletions, insertions and/or additions that may be made to a highly homologous sequence to SEQ ID NO:2 or to the non-mutated SEQ ID NO:19. The active site is identified in Figure 10" (page 23, last paragraph, through page 24).

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This is not agreed with because the claimed invention must be described in the specification not in the art. Further, even if the active site residues for SEQ ID NO:19 are known, the claimed invention is drawn not just to active pyruvate carboxylase but to a mutant with the specific property such as resistance to feedback inhibition by aspartic acid, said specific property absent in the wild-type enzyme. This property is the distinguished attribute common to the all members of the claimed genus. Furthermore, the examiner agrees with Applicant that "claim should specify a limit on the number of amino acid substitutions, deletions, insertions and/or additions that may be made to a sequence", supra. However, as explained in the rejection above, there is no structural limitations in claims.

Applicant further refers to SEQ ID NO: 6, 8, 10, 12, 14, 16 and 18 and asserts that "Applicant has disclosed seven(7) fragments which impart the altered activity of the pyruvate carboxylase of the invention" (page 25). This is not agreed with because of the following. SEQ ID NOs: 6, 8, 10, 12, 14, 16 and 18 are each 13-18 amino acids long and comprise one of the seven specific mutations in SEQ ID NO:2. However, SEQ ID NO:2 is 1157 and said fragments constitute about 1% of its structure. The recited structural feature of the genus (i.e., comprise the sequence of SEQ ID NOs: 6, 8, 10, 12, 14, 16 or 18) does not constitute a substantial portion of the genus as the remainder of the structure of a polypeptide with the pyruvate carboxylase desensitized to feedback inhibition by aspartic acid activity is completely undefined. Fragments

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consisting of 13-18 amino acids of SEQ ID NO:2 are highly unlikely to impart the requisite activity and the claim does not define the remaining structural features necessary for members of the genus to be selected. Moreover, Appendix A of the amendment shows said fragments as simultaneously fragments of SEQ ID NO:2 and SEQ ID NO:19 whereas they are fragments of SEQ ID NO:2.

With regard to the enablement rejection, Applicant argues that Modak and Attwood references provide information on the structure of pyruvate carboxylases albeit from different species (pages 26-27).

This is not persuasive because while methods to produce variants of a known sequence such as site-specific mutagenesis, random mutagenesis, etc. are well known to the skilled artisan producing variants as claimed by applicants (i.e., encoding a mutant pyruvate carboxylase that is desensitized to feedback inhibition by aspartic acid) requires that one of ordinary skill in the art know or be provided with guidance for the selection of which of the infinite number of variants have the claimed property. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. This would clearly constitute **undue** experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has **not** been provided in the instant

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specification. As previously stated the specification does not establish: (A) regions of the protein structure which may be modified without effecting pyruvate carboxylase activity and feedback inhibition by aspartic acid; (B) the general tolerance of pyruvate carboxylases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any pyruvate carboxylase residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Applicant's arguments regarding the 112, 2nd paragraph, rejection are moot in view of the amendment.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

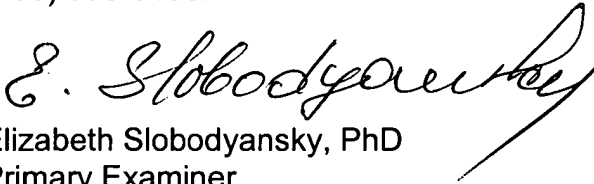
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shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky whose telephone number is (703) 306-3222. The examiner can normally be reached Monday through Friday from 9:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX phone number for Technology Center 1600 is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Center receptionist whose telephone number is (703) 308-0196.

A handwritten signature in cursive script, appearing to read 'E. Slobodyansky', with a long, sweeping horizontal stroke extending to the right.

Elizabeth Slobodyansky, PhD
Primary Examiner

November 20, 2003